SECTION II
REMARKS

Regarding the Amendments

Claims 3, 8, 12, 13, 22, 23 and 40 have been amended as set forth in the above Complete Listing of the Claims. As amended, the claims are supported by the specification and the original claims. No new matter has been added, as defined by 35 U.S.C. § 132.

Thus, upon entry of the amendments, claims 3-16, 22-28, 32, 37 and 40 will be pending, of which claims 12-16, 22-28, 32, 37 and 40 are withdrawn.

Rejection of Claims Under 35 U.S.C. §112

Definiteness

In the Office Action mailed May 21, 2008, the examiner has rejected claims 3-11 as indefinite. Specifically the examiner has rejected the claims for containing the phrase "sequences set forth in SEQ ID NO: 1..." in claim 3 and claims 4-7 are rejected for depending from claim 3. The examiner's attention is respectfully drawn to the amended claims as set forth in Section I above, where claim 3 has been amended such that it no longer contains the rejected phrase. As amended, claim 3 contains a proper Markush group, referring to SEQ ID NOs: 1-6 as the selection species.

Additionally the examiner has rejected claim 8 and claims 9-11 dependent therefrom as indefinite for recitation of the phrases "from about 15 to about 21 amino acid residues from the amino terminus region of HIV Tat" and "wherein the amino acid sequence comprises at least amino acid residues 1, 7, and 12." Applicants respectfully disagree.

It is clear from both the claim language and the specification (p. 4, ll. 18-22) that the claimed vaccine comprises a peptide of about 15-21 amino acids in length, where the peptide contains all of amino acid residues 1, 7 and 12 from the amino-terminal end of HIV Tat. In order to further clarify this subject matter, claim 8 has been amended, however, the scope of the claim remains the same.

It is respectfully submitted that pending claims 3-11 are clear and definite, as required in 35 U.S.C. §112, second paragraph. Withdrawal of the rejection is therefore respectfully requested.

Enablement

Claims 3 and 8-11 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement of that section. Claim 3 recites a therapeutic composition and claims 8-11 recite a therapeutic vaccine. It is the examiner's allegation that these claims are not enabled by the specification, as filed. Applicant respectfully disagrees.

Specifically, the examiner applies the *In re Wands* factors to the analysis of the lack of enablement of rejected claims 3 and 8-11. Applicants submit that an analysis of such factors leads to the conclusion that one of skill in the art would have been enabled to obtain the claimed therapeutic compositions/vaccines. The examiner alleges that analysis of the *In re Wands* factors "Nature of the Invention," "State of the Art," "Guidance in the Specification" and "Working Examples" are insufficient to provide enablement to claims 3 and 8-11. The examiner states that "[a]pplicants have not provided sufficient guidance to allow one skilled in the art to make and use the claimed invention with a reasonable expectation of success and without undue experimentation." (Office Action mailed May 21, 2008, page 11.) Applicant respectfully disagrees.

- Nature of the Invention

In a statement regarding the nature of the invention, the examiner states that "nature of the invention in claim 3 is a therapeutic composition comprising a fragment of SEQ ID NO: 1, 2, 3, 4, 5 or 6, which can be as small as a peptide of three amino acids." (Office Action mailed May 21, 2008, page 5.) The examiner's attention is respectfully drawn to the language of claim 3 as set forth in Section I above. As amended, the claim does not encompass fragments of any of SEQ ID NO: 1-6, but the full length peptides of those sequences. It would not require undue experimentation to use one of the six recited peptides in a composition of claim 3.

Regarding claims 8-11, the examiner states that "the specification does not sufficiently support the full scope of the claimed vaccine." (Office Action mailed May 21, 2008, page 6.) Applicants respectfully disagree. The claim, as amended and as discussed under the "Definiteness" heading above clearly recites a peptide of about 15-21 amino acids in length, where the peptide contains all of amino acid residues 1, 7 and 12 from the amino-terminal end of HIV Tat. This is supported in the specification, for example, at p. 4, ll. 18-22.

The claims recite a therapeutic composition/vaccine which, by definition, is administered to establish immunity to a disease. The claimed therapeutic compositions/vaccines have such established therapeutic effect, demonstrated by expression of antibodies to the peptide and blocked uptake of tat.

- State of the Art

In describing the "State of the Art," the examiner states that "…nearly any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined." (Office Action mailed May 21, 2008, page 6.)

It is respectfully submitted that by the guidance in the specification and working examples, provided in the application, as discussed below, the prophylactic nature of the administration reaction is demonstrated in both the detection of antibodies generated against Tat and a showing of blocked uptake and transactivation of tat.

- Guidance in the Specification and Working Examples

It is well established that

> "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (CCPA 1970)." (MPEP §2164.01(b); emphasis added.)

The elements of the claimed composition/vaccine of claims 3 and 8-11, namely the recited peptides are clearly set forth in the specification. Specifically, the peptides are described at pages 4-9 in the "Summary of the Invention" section; at pages 12-13, under the heading "Isolated and Purified Polynucleotides that Encode Tat Amino Terminus Linear Epitope Peptides;" at pages 15-19, under the heading "A Tat Amino Terminus Linear Epitope Peptide;" at pages 28-29, under the heading "Pharmaceutical Compositions." As such the makeup of the claimed compositions/vaccines is clearly disclosed.

Furthermore, on page 38 in the Examples section, it is reported that "…sera from immunized macaques or mouse monoclonal antibodies blocked Tat uptake by Jurkat cells. Incubation of recombinant Tat with monoclonal anti-Tat antibodies directed against aa 1 to 15

(TR1)....inhibited the accumulation of Tat..." and that "[m]onoclonal antibodies 9A11 and TR1...strongly neutralized the transactivation activity of Tat protein..." As such, the use of the claimed compositions/vaccines is clearly disclosed and is further supplemented in other portions of the specification, for example, at pages 28-29, where it is discussed in detail how the peptides can be combined with a carrier and how the resulting composition can be administered.

One of skill in the art would have properly viewed the teachings of the specification as a whole and would have found the totality of such teachings to be reasonably predictive of the efficacy of the peptides in a therapeutic composition/vaccine, as claimed.

Accordingly, withdrawal of the rejection of claims 3 and 8-11 for lack of enablement under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection of Claims Under 35 U.S.C. §103

In the Office Action mailed May 21, 2008, the examiner rejected claims 3-7 under 35 U.S.C. § 103 as unpatentable over U.S. Patent No. 5,652,122 (hereinafter "Frankel et al."). Applicants respectfully disagree.

It is elemental law that in order for an invention to be obvious, the difference between the subject matter of the application and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard for a proper §103 rejection, all claim limitations must be disclosed or derivable from the cited combination of references, there must be a logical reason to combine the cited references to produce an operable combination and there must be a reasonable expectation of success. (MPEP §2143)

Specifically the examiner alleges that it would have been obvious to one of skill in the art to obtain the claimed composition from Frankel et al.'s disclosure of a composition comprising a pharmaceutically acceptable carrier and a molecule of interest. Applicants respectfully disagree.

Initially, the examiner's attention is respectfully drawn to the language of claim 3 as set forth in Section I above. Claim 3 recites: "A therapeutic composition comprising at least one peptide having an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID

NO:2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6" Each of SEQ ID NOs: 1-6 is 21 amino acids long.

By contrast, SEQ ID NO: 7 of Frankel et al., cited by the examiner comprises 56 amino acids, termed tatΔcys and is Tat residues 1-21 fused directly to residues 38-72. The objective of the fusion peptides of Frankel et al. is "delivery of biologically active cargo molecules...accomplished by the use of novel transport polypeptides which comprise HIV tat protein..." (Frankel et al., Abstract) Cargo molecules are defined in Frankel et al. as "[a] molecule that is not a tat protein or a fragment thereof, and that is either (1) not inherently capable of entering target cells, or (2) not inherently capable of entering target cells at useful rate..." (Frankel et al. col. 5, ll. 37-40.) One of skill in the art would not use the description of Frankel et al. to generate the claimed therapeutic compositions, as the tat fragments in Frankel are used to mediate entry of other proteins into a cell. Indeed, Frankel et al. even describes inclusion of stabilizing agent (col. 6, ll. 45-50) "which serves to increase tat stability and uptake." (emphasis added) The present invention, by contrast, is directed to administration of the tat peptides in order to elicit antibodies that will neutralize the biological activity of Tat internalization in T cells.

Where Frankel et al. provide a tat conjugate in order to assist entry of other proteins into cells, the present invention provides a therapeutic composition that blocks tat uptake and transactivation.

In considering a reference for its effect on patentability, the reference is required to be considered in its entirety, including portions of teach away from the invention under consideration. Simply stated, the prior art must be considered as a whole. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984); MPEP § 2141.02. "It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art." *Application of Wesslau*, 353 F.2d 238, 241 (C.C.P.A. 1965); *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 448 (Fed. Cir. 1986), cert. denied, 484 U.S. 823 (1987).

Frankel et al. teaches the essential nature of the inclusion of Tat amino acids 49-57 in a

polypeptide described therein (*See* Abstract, col. 3, ll. 24-40; col. 10, ll. 5-24; and Examples), states that "the amino acid sequence preceding the cysteine-rich region [per Abstract aa 22-36] of the tat protein is not required for cellular uptake" and provides that "[a] preferred transport polypeptide...consists of amino acids 37-72." (Frankel et al. col. 10, ll. 5-24) Frankel et al. therefore teach away from a peptide consisting only of amino acids 1-21, as are provided in SEQ ID NOs: 1-6.

As Frankel et al. does not provide any logical basis for the peptide such as that recited in the therapeutic composition of claim 3, Frankel et al. does not render the claimed invention obvious. Furthermore, as claims 4-7 depend from claim 3, by nature of that dependency they contain all elements of claim 3. Accordingly, Frankel et al. does not render claims 4-7 obvious. Withdrawal of the rejection of claims 3-7 under 35 U.S.C. § 103 (a) as being obvious over Frankel et al. is respectfully requested.

CONCLUSION

All of Applicants' pending claims 3-11 are patentably distinguished over the art, and in form and condition for allowance. The Examiner is requested to favorably consider the foregoing and to responsively issue a Notice of Allowance.

Rejoinder of withdrawn claims 12-16, 22-28, 32, 33, 37 and 40 is requested under the provisions of MPEP 821.04.

The time for responding to the May 21, 2008 Office Action without extension was set at three months, or November 21, 2008. Applicants hereby request a 3 month extension of time under 37 CFR § 1.136 to extend the deadline for response to and including November 21, 2008. Payment of the extension fee of $555.00 specified in 37 C.F.R. § 1.17(a)(3), as applicable to small entity, is being paid by on-line credit card payment at the time of EFS submission of this Response. Should any additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the Examiner is requested to contact the undersigned attorneys at (919) 419-9350 to discuss same.

Respectfully submitted,

Date: November 21, 2008

/steven j. hultquist/
Steven J. Hultquist
Reg. No. 28,021
Attorney for Applicants

Date: November 21, 2008

/kelly k. reynolds/
Kelly K. Reynolds
Reg. No. 51,154
Attorney for Applicants

INTELLECTUAL PROPERTY/ TECHNOLOGY LAW
Phone: (919) 419-9350
Fax: (919) 419-9354
Attorney File No.: 4115-194

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